

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP2004/014310

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHINNAIYAN A M ET AL.: "Molecular signatures of sepsis. Multiorgan gene expression profiles of systemic inflammation"</p> <p>AMERICAN JOURNAL OF PATHOLOGY, vol. 159, October 2001 (2001-10), pages 1199-1209, XP008037039</p> <p>cited in the application</p> <p>* siehe speziell Abb.2-5 *</p> <p>the whole document</p> <p style="text-align: center;">----- -/-</p>	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

30 August 2005

Date of mailing of the international search report

05/09/2005

Name and mailing address of the ISA

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International Application No  
PCT/EP2004/014310

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PATHAN N ET AL.: "The complexity of the inflammatory response to meningococcal sepsis revealed by gene expression profiling using cDNA microarrays" CRITICAL CARE MEDICINE, vol. 30, no. 12, December 2002 (2002-12), page A47, XP008037050 abstract	
A	WIEGAND G ET AL.: "Gene expression pattern in human monocytes as a surrogate marker for systemic inflammatory response syndrome (SIRS)" MOLECULAR MEDICINE, vol. 5, 1999, pages 192-202, XP008037023 * siehe insbesondere Abb.3 * the whole document	
P,X	US 2004/096917 A1 (IVEY RICHARD M ET AL) 20 May 2004 (2004-05-20)  abstract page 4, column 1, paragraph 32 page 7, column 2, paragraph 63 page 25, column 2, paragraph 156; claims 4,8,10,20-22,42,47,82,84,88; figure 5; tables 15,16	1,4,6,7, 9-11,19, 20
P,Y	WO 2004/087949 A (SIRS-LAB GMBH; RUSSWURM, STEFAN; REINHART, KONRAD; SALUZ, HANS-PETER;) 14 October 2004 (2004-10-14) cited in the application the whole document	1-15, 18-25
P,Y	PRUCHA M ET AL.: "Expression profiling: Toward an application in sepsis diagnostics" SHOCK, vol. 22, no. 1, July 2004 (2004-07), pages 29-33, XP008036997 the whole document	1-15, 18-25

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International application No.

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## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 16, 17, 26-32  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## Continuation of II.2

Claims: 16, 17, 26-32

The current claim 1 relates to a method defined by a desirable characteristic or property, namely the use of "at least one DNA that has specific gene activity for distinguishing between SIRS and sepsis...or is a specific gene or gene fragment therefor" (see *inter alia* parts b) and d) of claim 1). According to the description (*inter alia* tables in the examples), such "gene activity" is to be understood as an altered gene expression pattern in comparison between SIRS and sepsis.

Claim 1, as claimed, therefore comprises all nucleic acid sequences whose expression patterns appear suitable for distinguishing SIRS and sepsis, individually or in any combination. However, the description supports and discloses within the meaning of PCT Article 5 only methods which use the in total 68 genes or gene fragments indicated in Table 2 (increased gene activity of 51 specified genes) and Table 3 (reduced gene activity of 17 specified genes). Beyond that the application provides neither support for nor disclosure of other genes. To a person skilled in the art it thus remains unclear what other genes (other than the genes specified in in Tables 2 and 3) are suitable for such a method or such a test, or by what criteria they can be selected for use in such a method. This also applies to the other 23 genes of the Seq. Id. Nos. specified in dependent claim 10 which are not mentioned in Tables 2 and 3.

Further, dependent claims 16, 17, 20 and 21 claim "synthetic analogs, aptamers as well as peptido nucleic acids" (claims 16 and 17) and "enzymatic or chemical derivatives" (claims 20 and 21) derived from the specified genes or their RNA, with no indication anywhere in the application as to what specific analogs, aptamers or peptido nucleic acids or enzymatic or chemical derivatives were meant.

Therefore, the search concerning claims 1-25 was limited to the parts that appear to be clear, supported and disclosed in the above sense, in particular a method according to claim 1 using the genes specified in Tables 2 and 3 (in relation to claim 10 and other claims dependent thereon) as well as

dependent claims 2-15, 18, 19, 20 (in part), 21 (in part) and 22-25.  
Dependent claims 16 and 17 were not searched.

Use claims 26-32 also fail to meet the PCT requirements as they do not show the clarity stipulated in PCT Article 6. Instead, they attempt to define the claimed use in terms of the desired results, that is:

Claim 26: "use of specific nucleic acids...as calibrators...and/or for assessing effect and toxicity...and/or for the manufacture of therapeutic agents"

Claim 27: "use of the RNA...for obtaining quantitative information on gene activity by means of hybridization-dependent procedures"

Claim 28: "use of gene activities...for screening active agents in model organisms"

Claim 29: "use of gene activities...which are modeled at the cellular level by gene activities"

Claim 30: "use of the genes...to obtain information...for further electronic processing"

Claim 31: "use of gene activity data for the production of software for diagnostic purposes and/or patient data management systems"

Claim 32: "use of gene activity data for the production of expert systems for modelling cellular transmission paths".

In the absence of essential features that would give claims 26-32 the requisite clarity under PCT Article 6, it is not possible to carry out a meaningful search covering the entire range of protection sought. Therefore, these claims were not searched.

The applicant is advised that claims relating to inventions in respect of which no international search report has been established normally cannot be the subject of an international preliminary examination (PCT Rule 66.1(e)). In its capacity as International Preliminary Examining Authority the EPO generally will not carry out a preliminary examination for subjects that have not been searched. This also applies to cases where the claims were amended after receipt of the international search report (PCT Article 19) or where the applicant submits new claims in the course of the procedure under PCT Chapter II. After entry into the regional phase before the EPO, however, an additional search can be carried out in the course of the examination (cf. EPO Guidelines, Part C, VI, 8.5) if the deficiencies that led to the declaration under PCT Article 17(2) have been remedied.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/014310

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004096917 A1	20-05-2004	AU 2003291482 A1	03-06-2004
		AU 2003291483 A1	03-06-2004
		AU 2003291484 A1	03-06-2004
		AU 2003291488 A1	03-06-2004
		EP 1565570 A2	24-08-2005
		WO 2004044554 A2	27-05-2004
		WO 2004044555 A2	27-05-2004
		WO 2004044556 A2	27-05-2004
		WO 2004043236 A2	27-05-2004
		US 2004097460 A1	20-05-2004
		US 2004106142 A1	03-06-2004
		US 2004157242 A1	12-08-2004
WO 2004087949 A	14-10-2004	DE 10315031 A1	14-10-2004
		DE 10336511 A1	24-02-2005
		DE 10340395 A1	17-03-2005
		WO 2004087949 A2	14-10-2004